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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 05/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/232,880	XU ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-30 and 34-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-30 and 34-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 16, 2003 has been entered.

2. Claims 27-30 and 34-37 are pending.

Claims 1-6, 8, 9 and 11-25 have been canceled.

Claims 27-30 and 34-37 have been amended.

Claims 27-30 and 34-37 are examined on the merits.

Claim Objections

3. Claim 1, line 5 is objected to because of the following informality: the word "polynuceotide" should be replaced with "polynucleotide". Correction is required.

Maintained and New Grounds of Rejection

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 34-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Applicants have amended claims 34-37 to include new method steps comprising contacting a biological sample *with at least two oligonucleotide primers in a PCR, wherein said primers are specific for an expressed polynucleotide sequence that comprises SEQ ID NO: X* followed by detecting in the sample an amount of a polynucleotide *that amplifies in the presence of the said primers*, repeating these steps and comparing the amount of polynucleotide in order to monitor the progression of the cancer in a patient.

Applicants assert support for these amendments are found in the specification at page 38, lines 6-11. The Examiner has reviewed this section of the specification and it is clear these method steps are supported in the context of determining the presence or absence of prostate cancer in a patient, but not in the context of monitoring the progression of cancer in a patient. There appears to be no contemplation of the recited method steps in the realm of assessing the progression of any cancer including prostate. Applicants are requested to delete the new matter or explicitly cite where in the specification support can be found.

6. Claims 37-30 and 34-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method, which rely on the amplification of a portion of an expressed polynucleotide that comprises SEQ ID NO: 67, 107, 308 or 311. The claims do not read on an amplified product of the expressed polynucleotide sequences which is the full length sequence of SEQ ID NO: 67, 107, 308 or 311, therefore the written description is not commensurate in scope with claims which read on a genus of sequences that comprise a fragments of SEQ ID NO: 67, 107, 308 or 311.

The specification does not describe with any degree of particularity a single member of the genus of polynucleotide sequences obtained from the PCR process utilizing oligonucleotide primers specific for expressed polynucleotide sequences comprising SEQ ID NO: 67, 107, 308 or 311. The method reads on portions of amplified polynucleotides.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date

> sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has

Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of polynucleotides, which are amplified the skilled artisan could not immediately recognize or distinguish members of the polynucleotides within the claimed method. One skilled in the art would not recognize that Applicant had possession of the claimed invention at the time the application was filed. There is insufficient support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

The full breadth of the claims does not meet the written description provision of 35 U.S.C. 112, first paragraph.

7. The rejection of claims 27-30 and 34-37 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained. Claims 8, 9, 11 and 12 have been cancelled.

Applicants argue specific structures of polynucleotide sequences of SEQ ID NO: 67, 107, 308 and 311 have been identified and these sequences exhibit prostate cancer-associated expression profile and a skilled artisan would have no difficulty using the sequences for detecting the said sequences in a biological sample and the detection

of prostate cancer, see page 7 of the Remarks. Applicants assert "...the design and use of polynucleotide primers and probes having hybridization specificity for a target polynucleotide sequence is well described by the...specification", see page 8. These arguments have been carefully considered but found unpersuasive.

Applicants' disclosure has not sufficiently provided parameters, which define or characterize the oligonucleotides germane to the claimed invention. Parameters such as the structure, the size, as well as the sequence of the oligonucleotides, are necessary in order to practice the claimed invention. The breadth of the scope of the broadly claimed method embodies any and all nucleotide fragments capable of binding to Applicants' target sequences (SEQ ID NO: 67, 107, 308 and 311), thereby not precluding fragments, which are not prostate specific. While Applicants point the Examiner's attention to page 6, line 21-page 14, line 17 of the specification this section of the disclosure is prophetic. There is insufficient guidance supporting the implementation of the two oligonucleotide primers in a PCR in methods for determining the presence or absence of prostate cancer and monitoring the progression of a cancer, which has not been limited my cancer type, organ type or type of cancer (i.e. hematopoietic or solid.) The method of monitoring the progression of a cancer in a patient as noted in the new matter rejection is not supported in the specification notwithstanding the specification only seems to discuss detecting sequences for the diagnosis of prostate cancer and no other types of cancer. Moreover, the specification has not provided sufficient guidance as to which regions of the target sequences are specific to diagnosing prostate cancer and to which the oligonucleotides must hybridize

in order to make a discriminate prostate cancer diagnosis. The specification does not suitably provide information as to how to design these fragments establishing its sequence or structural characterization and how to screen for these oligonucleotides. And while the Examiner concurs with the Applicants' assertion that short fragments, such as 20 nucleotides are routinely used to determine expression levels germane to Applicants' invention of diagnosis, the size of the fragment is not relevant. The structure and sequence of the oligonucleotides that aid in the method of diagnosis of prostate cancer is significant and guidance must be provided as to how to make such oligonucleotides.

Based on the analysis and the teachings presented above and of record it would require undue experimentation for the skilled artisan to practice this invention because there is no support in the specification for the enablement of the broadly claimed invention regarding the oligonucleotides used in the claimed methods. Therefore, in view of the insufficient guidance in the specification, extensive experimentation would be required to enable the claims and to practice the invention as claimed.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 27-30 and 34-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The claims recite implementing at least two oligonucleotide primers in PCR wherein the said primers are specific for an expressed polynucleotide sequence that comprises SEQ ID NO: X (can be 67, 107, 308 or 311). It seems as if while one primer is specific for the said sequence it is not clear what the other primer is specific for. Therefore, the metes and the bounds cannot be determined.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571) 272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
01 May 2006